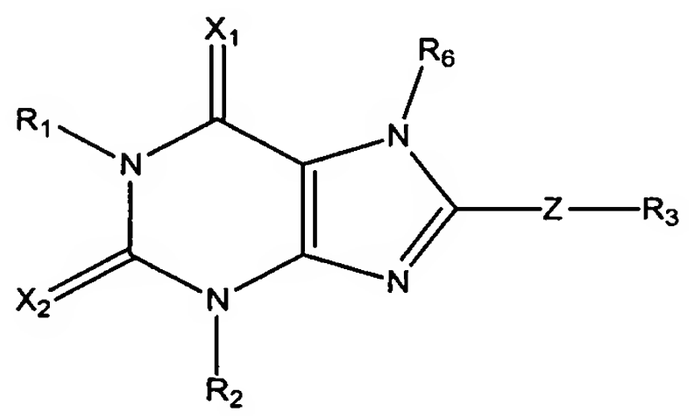
Amendments to the Specification:

Please replace the Abstract with the following amended Abstract:

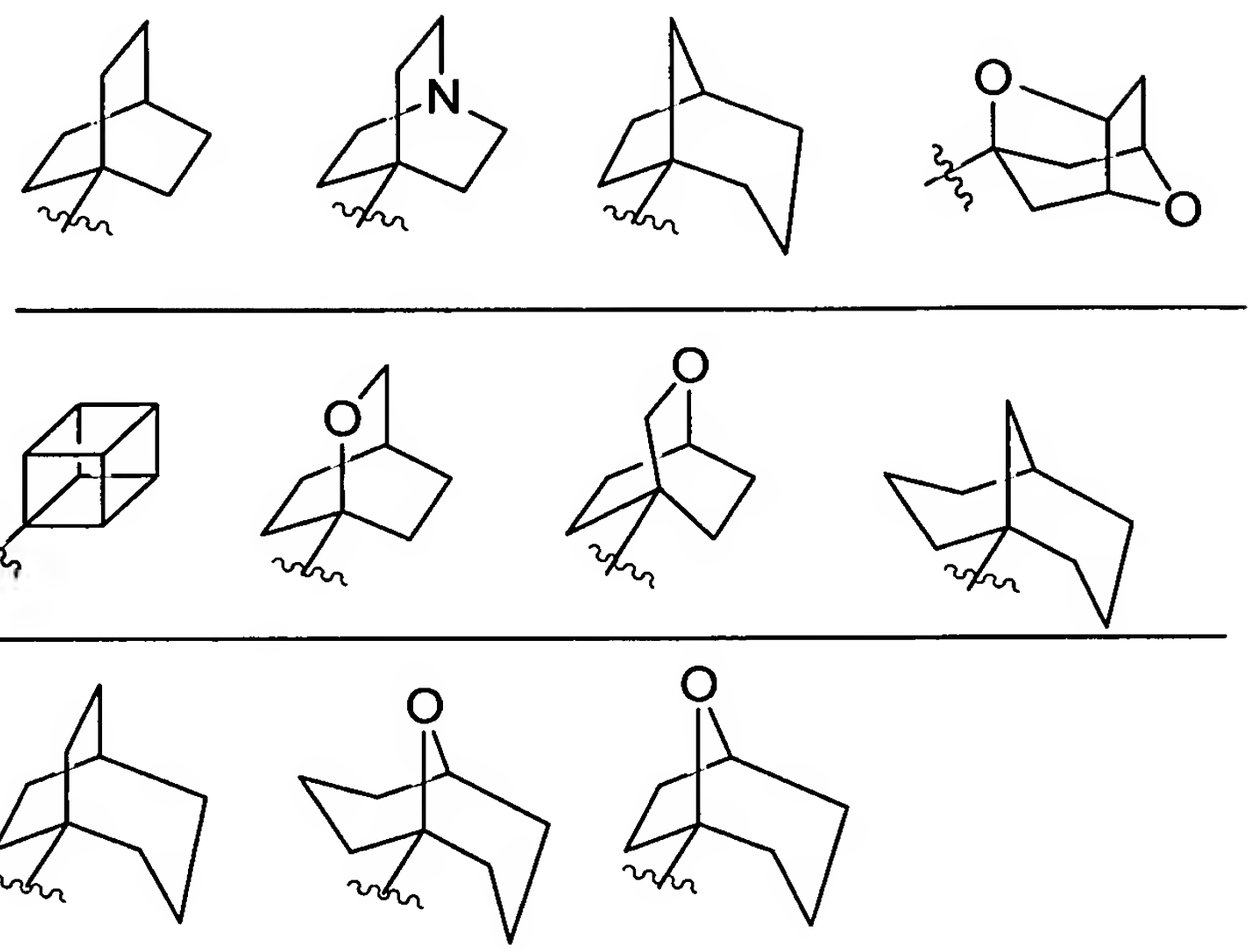
The invention is based on the discovery that compounds of Formula I are unexpectedly highly potent and selective inhibitors of the adenosine A_1 receptor. Adenosine A_1 antagonists can be useful in the prevention and/or treatment of numerous diseases, including cardiac and circulatory disorders, degenerative disorders of the central nervous system, respiratory disorders, and many diseases for which diuretic treatment is suitable.

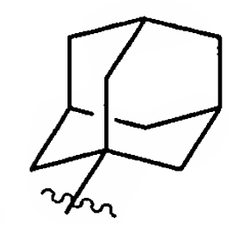
In one embodiment, the invention features a compound of formula I:



(I),

wherein $\mathbf{R_3}$ is an optionally substituted bicyclic, tricyclic or pentacyclic group selected from the group consisting of:

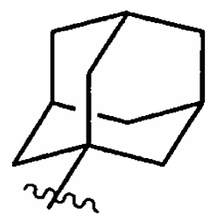




or a substituted ; and wherein R_1, R_2, R_4, R_5, R_6, X_1, X_2 and Z are as described in the specification.

Please replace lines 6-9 on page 4 with the following:

(b) the tricyclic group:



where the tricyclic group is functionalized with one or more ~~substitents~~ substituents selected from the group consisting of:

Please replace the first paragraph, lines 1-15 on page 17 with the following:

There are many methods to further functionalize compound (J), which contains a carboxylic acid or ester attached to the R_3 moiety. For example, compound (J) can be converted to the corresponding acrylic acid derivative. One way is to first hydrolyze the ester group of compound (J) (provided that R_a is not H) to give the corresponding carboxylic acid, reduce the carboxylic acid to the corresponding alcohol, oxidize the alcohol to the corresponding aldehyde, and then perform a Wadsworth-Horner-Emmons or Witting reaction to form the corresponding acrylic acid derivative. See, e.g., Examples 5, 6, 15, 16, and 17. Compound (J) can also be transformed directly to its corresponding alcohol (see, e.g., Example 4). A different variation is to transform compound (J) directly to its corresponding aldehyde. A further variation, is to transform an ester-containing compound (J) to its corresponding carboxylic acid, and then directly to the aldehyde. Alternatively, one can functionalize the precursor compound of the $Z\text{-}R_3$ moiety before coupling to the ~~or~~ 1,3-disubstituted-8-unsubstituted xanthine in scheme 1 or the 1,3-disubstituted-5,6-diaminouracil in scheme 2. Further, compounds of this invention can be prepared on solid support (e.g., Wang resin). See Example 36.

Please replace the paragraph bridging pages 17-18 with the following:

FIG. 4 discloses an alternative processes for the transformation of compound (VII) to the corresponding alcohol (X) and the subsequent transformation of the alcohol (X) to the olefin (XII). Steps (F') thru (H) are ring closure followed by soponification of the ester (VIII) to the acid (IX) followed by reduction to the alcohol (X), see Examples 84, 85, and 86.

Alternatively, compound (VII) can undergo reduction (step (Y), see Example 103) and cyclization reactions to produce compound (X) (step (Z), see, e.g., Example 84a). A further alternative way involves soponification and cyclization of compound (VII) to produce compound (IX) (steps (Y') and (Z')). These reactions are well known to those skilled in the art. See, e.g., Examples 85a and 84a. Steps (I) thru (DD) disclose ~~alterntive~~ alternative processes for the transformation of the alcohol (X) to the corresponding olefin (XII). Specifically, steps (J), (AA) and (CC) (see Examples 89, 104, and 105) are alternative ways of transforming the one carbon aldehyde of compound (XI) to the acrylic acid/ester-containing moiety by means known to those skilled in the art.

Please replace lines 25-28 on page 24 with the following:

The resulting acid was dissolved in ~~of~~ acetic anhydride (3 ml) and refluxed for 1 h. It was then cooled to RT and concentrated. The resulting residue was dissolved in EtOAc and washed with sat'd. aq. $NaHCO_3$, brine, dried (Na_2SO_4), and concentrated. Purification by chromatography (2:1 EtOAc/hex) afforded the title compound. MS (ES^+) 361.

Please replace lines 18-28 on page 25 with the following:

4-Oxo-cyclohexanecarboxylic acid ethyl ester was converted to the corresponding ketal derivative according to an established procedure (Greene, *Protective Groups in Organic Synthesis, Third Edition*). This ketal derivative (1.0 g, 4.67 mmol) was dissolved in anhydrous THF (15 ml). In a separate flask, 2,2,6,6-tetramethylpiperidine (1.2 ml, 1.5 eq) was dissolved in ~~of~~ THF (30 ml) and cooled to –78°C and nBuLi (2.80 ml, 2.5 M solution in hexanes, 1.5 eq) was added. After 15 min, the ketal solution was added and the reaction

mixture was stirred at –78°C for 1 h. Methyl chloroformate (0.72 ml, 2 eq) was added and the reaction mixture was warmed to RT. The reaction was quenched with sat'd. aq. NH_4Cl and extracted with EtOAc. The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. Purification by chromatography (2:1 hex/EtOAc) afforded the diester intermediate.

Please replace lines 3-4 on page 44 with the following:

Example 27d: ~~27d:~~ 3-(4-{3-[2-(4-Hydroxy-phenyl)-ethyl]-2,6-dioxo-1-propyl-2,3,6,7-tetrahydro-1H-purin-8-yl}-bicyclo[2.2.2]oct-1-yl)-propionic acid, (MH^+= 495.12).

Please replace lines 11-22 on page 69 with the following:

To a stirred suspension of methyl triphenylphosphonium chloride (1.07 g, 3.0 mmol) in THF (20 ml) at 0°C was added n-BuLi (1.4 M in hexane, 2.14 ml, 3.0 mmol). The resulting reddish-brown mixture was stirred at this temperature for 0.5 h and then at rt for 0.5 h. A solution of 4-(2,6-dioxo-1,3-dipropyl-2,3,6,9-tetrahydro-1H-purin-8-yl)-bicyclo[2.2.2]octane-1-carbaldehyde (372 mg, 1.0 mmol) in THF (10 ml) was added over a period of 20 minutes and the resulting mixture was stirred overnight (12 h). The reaction mixture was partitioned between saturated aqeuous NH_4Cl (20 ml) and EtOAc (20 ml) and the aqueous phase was extracted with EtOAc (20 ml). The combined organic extracts were washed with saturated ~~aqeuous~~ aqueous NaCl (50 ml), dried ($MgSO_4$), filtered and evaporated *in vacuo* to afford an oil that was purified by radial chromatography (2 mm plate) using a gradient of 0-5% MeOH in CH_2Cl_2 as eluent. Product-containing fractions were combined and concentrated to afford 140 mg (38%) of a white solid. MS: 371 (MH^+).

Please replace the paragraph bridging pages 85-86 with the following:

To a stirred solution of diisopropylamine (84.5 ml, 600 mmol) in THF (anhydrous, 700 ml) cooled to –30°C under nitrogen is added *n*-butyl lithium (2.5 M in hexane, 220 ml, 550 mmol) by a syringe. The ~~misture~~ mixture is stirred for 30 min at –30°C and then cooled to –78°C. HMPA (360 ml, 4 equivalents, 2 mol) is added by a syringe and a ~~dolution~~ solution of dimethyl cyclohexane-1,4-dicarboxylate (100 g, 500 mmol) in THF (anhydrous, 100 ml is added by a syringe subsequently. The mixture is stirred for an additional 40 min. Then 1-bromo-2-chloroethane (41.5 ml, 500 mmol) is added and the mixture stirred at –78°C for an additional 20 min. The cold bath is removed and stirring is continued for 1 hr. The reaction mixture is cooled back to –78° and a mixture of HMPA (360 ml, 4 eq, 2 mol) in THF 600 ml) is added. By cannula, freshly prepared LDA (200 ml of *n*-butyl lithium, 2.5 M in hexane, 500 mmol is added to diisopropylamine (78 ml, 556 mmol) in THF (anhydrous, 700 ml)) is transferred into the reaction mixture at –78°. The reaction mixture is stirred at –78° for 1.33 hr followed by removal of the cooling bath and additional stirring for 5-6 hr. The mixture is quenched with saturated aqueous ammonium chloride (400 ml) and concentrated under reduced pressure at 35° to remove the THF. The residue is diluted with water (800 ml) and extracted with hexance (3 x 600 ml). The combined extracts are washed with saline (700 ml) and dried over sodium sulfate. Using a bath temperature of 35° the solvents are ~~are~~ removed under reduced pressure to give a residue. The residue is stirred with hexane (50 ml) at 20-25° for 0.5 hr. The resulting suspension is cooled to 0° for 2 hr and filtered to give the title compound.